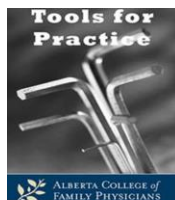


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**[\(en français\)](#)**



## **Hydrochlorothiazide and Squamous Cell Skin Cancer: Remember when hypertension was easy?**



**Clinical Question: Does hydrochlorothiazide increase the risk of squamous cell carcinoma (SCC) of the skin?**

**Bottom Line: Observational data suggest an association between hydrochlorothiazide and the risk of SCC. Causation has not been proven. Risk appears to consistently increase with dose and duration (example: 5 years of use increases risk 3-4 times). Baseline incidence of SCC is <0.1% annually. The same risk has not been established with thiazide-like diuretics (like indapamide or chlorthalidone). The benefit of switching from hydrochlorothiazide to another agent should be weighed against the risk of changing medications.**

### **Evidence:**

- Statistically significant unless indicated.
  - Systematic review:<sup>1</sup> 2 cohort and 7 case-control studies (395,789 patients).
    - Association of SCC with thiazide diuretics: Odds Ratio (OR)=1.9
      - Subgroup analysis:
        - Hydrochlorothiazide and hydrochlorothiazide combinations consistently increased SCC risk: OR=2.
        - Long-term HCTZ use (≥4.5 years) associated with higher SCC risk OR=3.3
      - Limitations: potential unmeasured confounders; recall and detection bias; multiple comparisons.
    - Largest case-control study<sup>2</sup>, not in above systematic review: 80,162 SCC cases in Denmark matched with 1,603,345 controls.
      - Hydrochlorothiazide ≥50,000mg cumulative dose (~6 years use) associated with SCC risk: OR=4.
      - Consistent dose-response relationship observed for SCC: OR=7.4 with hydrochlorothiazide ≥200,000mg cumulative dose (~20 years use).
    - Hydrochlorothiazide associated with risk of SCC lip cancer<sup>3</sup>:
      - Dose-response effect observed: OR=7.7 with ≥100,000mg cumulative dose.
    - Another systematic review<sup>4</sup> reported no effect with thiazides but did not include studies reporting on hydrochlorothiazide alone.
    - Basal cell carcinoma risk very small (OR=1.2-1.3), if real.<sup>1,2</sup>

**Context:**

- Baseline SCC risk varies with ethnicity, age, sex, and geographic location. A recent UK cohort reported an incidence of 77 cases per 100,000 people (<0.1%) per year.<sup>5</sup> Metastatic SCC developed in 1.1-2.4% of patients with SCC.<sup>6</sup>
- Non-randomized studies may overestimate beneficial and harmful effects and cannot prove causation.
- Thiazide and thiazide-like agents reduce morbidity and mortality in randomized controlled trials and are first line therapy in hypertension.<sup>7</sup>
- One hypertension society recommends thiazide-like diuretics as preferred initial option for hypertension (like chlorthalidone or indapamide), although suggest continuing hydrochlorothiazide in stable patients.<sup>8</sup>

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**Disclosures:**

Authors do not have any conflicts of interest to declare.

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